

Express Mail Label No. EV 159505489 US

Date of Deposit: August 26, 2003

Attorney Docket No: 21486-032DIV4

*Amdt B/#B*  
*9.10.03*



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

APPLICANTS: Wands et al.  
SERIAL NUMBER: 09/903,199 EXAMINER: Canella, K.  
FILING DATE: July 11, 2001 ART UNIT: 1642  
FOR: DIAGNOSIS AND TREATMENT OF MALIGNANT NEOPLASMS

**RECEIVED**  
SEP 07 2003  
TECH CENTER 1600/2900

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**AMENDMENT AND RESPONSE**

This paper is in response to the Office Action mailed on February 27, 2003. With a three month extension of time, the due date for response is August 27, 2003.

**Amendments to the Specification** begin on page 2 of this paper.

**Amendments to the Claims** are reflected in the listing of claims, which begins on page 4 of this paper.

**Remarks/Arguments** begin on page 6 of this paper.

On page 1, replace paragraph on lines 19-35 with the following paragraph.

61 The invention features a method for diagnosing a malignant neoplasm in a mammal by contacting a bodily fluid from the mammal with an antibody which binds to an human aspartyl (asparaginy) beta-hydroxylase (HAAH) polypeptide under conditions sufficient to form an antigen-antibody complex and detecting the antigen-antibody complex (for the purposes of this specification, HAAH polypeptide refers to the amino acid sequence of SEQ ID NO:2 and HAAH cDNA refers to the nucleotide sequence of SEQ ID NO:3). Malignant neoplasms detected in this manner include those derived from endodermal tissue, e.g., colon cancer, breast cancer, pancreatic cancer, liver cancer, and cancer of the bile ducts. Neoplasms of the central nervous system (CNS) such as primary malignant CNS neoplasms of both neuronal and glial cell origin and metastatic CNS neoplasms are also detected. Patient derived tissue samples, e.g., biopsies of solid tumors, as well as bodily fluids such as a CNS-derived bodily fluid, blood, serum, urine, saliva, sputum, lung effusion, and ascites fluid, are contacted with an HAAH-specific antibody.

On page 6, replace paragraph on lines 5-16 with the following amended paragraph.

62 For example, a compound which inhibits HAAH hydroxylation is a polypeptide that binds a HAAH ligand but does not transduce an intracellular signal or an polypeptide which contains a mutation in the catalytic site of HAAH. Such a polypeptide contains an amino acid sequence that is at least 50% identical to a naturally-occurring HAAH amino acid sequence or a fragment thereof and which has the ability to inhibit HAAH hydroxylation of substrates containing an EGF-like repeat sequence. More preferably, the polypeptide contains an amino acid sequence that is at least 75%, more preferably at least 85%, more preferably at least 95% identical to SEQ ID NO:2.

On page 47, lines 1-12, replace Table 4 with the following amended Table.

Table 4: Overexpression of enzymatically active HAAH  
indicates malignancy

Cdna	# of foci $\pm$ S.D. <sup>b</sup>	NIH 3T3 clone	# of colonies <sup>c</sup>
pcDNA3 (mock)	$6.0 \pm 3.3$	pcDNA (mock)	$0.4 \pm 0.5$
murine [H]AAH	$14.0 \pm 2.9$	clone 18 <sup>d</sup>	$6.2 \pm 2.9$
mutant murine [H]AAH <sup>a</sup>	$1.6 \pm 1.0$	clone 16 <sup>e</sup>	$4.7 \pm 6.5$
[human] HAAH	$32.0 \pm 5.4$		
v-scr	$98.0 \pm 7.1$		

a. enzymatically inactive [H]AAH

b.  $P < 0.01$  compared to mock and mutant murine [H]AAH

c.  $P < 0.001$  compared to mock

d. Clone 18 is a stable cloned NIH 3T3 cell line that overexpression human HAAH by approximately two fold.

e. Clone 16 is a stable cloned NIH 3T3 cell line that overexpresses human HAAH by about 50%.